

Hepatology 1

1 / 1

Liver is 1500 - 1700 g. has a 1.5 L of Blood Supply / min.

- Hard to get ischemic BC of the 2 double blood supply. 75% → Portal vein & 25% Hepatic A. oxygenated by ^{Red} S.O.

Sickle cell anemia & the pt. has tendency to sickle under certain conditions & stress.

Sickle cell crisis when the attack of sickling causes ischemia & necrosis of the tissues. & its one of the causes of liver ischemia.

- Liver has 8 lobes every lobe has a Blood vessel & artery & vein, & Bile duct so we can remove a whole lobe together.

- The Caudate lobe has 2 blood draining, & according to this fact we can dif. b/w liver congestion & causes if it was caused by occlusion of the Hepatic vein ~~not~~ or by Rt. Side HF with Raised JVP.
with Rt. side HF all of liver would be congested while in Budd-Chiari syndrome the Caudate lobe would be not congested.

VISIT...

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- Liver has bile & blood drainings, the bile also carries excretions & waste products.

- Blood enters space of dis by pressure of ~~dis~~ 10 mm/Hg leads to distention in hepatic sinusoid " it has high elasticity " but with chronic alcohol intake or inflammation " which heals with resolution in beginning but with fibrosis & organization " Ito cells synth. & secrete collagen results in fibrosis & ↓ elasticity
 ⇒ ↑ resistance ⇒ Portal HTN.

- Liver fibrosis is not the same as Cirro. & Fibrosis comes first.

- Dx of cirr. done by U/S ⇒ accurate & not invasive
 - Biopsy is a Gold Standard test but it isn't done any more " can't exclude cirr. & may be we biopsied the wrong site "

Dx. is done by $\nearrow$ Fibro scan "Fibro test"

It's a US, & accurate, measures the elasticity of space of this dis.

- if there was a mass a biopsy should be taken

- 75% of liver must be cirr. to become symptomatic & before it 75% liver cells can compensate.

- Not all pt. with liver cirr. has a liver failure

* There is a major 3 Q to evaluate liver failure

1- أغنى عليك من قبل لسبب غير معروف؟

2- من غير من قبل؟!

3- رجلك ويطنك انتخجو؟

Liver failure

"Hyper acute LF"

< 7 days.

"Acute LF"

"Acute in

top of chronic

Every hepatocyte has a small bile duct $\Rightarrow$ intra-hepatic Biliary system "Canaliculi" $\Rightarrow$ Lt. & Rt. hepatic duct $\Rightarrow$ Common Hepatic duct $\Rightarrow$ with Cystic duct $\Rightarrow$ Common bile duct

- The cells that line the biliary system ~~has~~ secrete Alkaline phosphatase.

While the Hepatocyte secrete 2 enzymes: AST & ALT GPT

ALP $\Rightarrow$ 45 - 115 IU

if > 2.5 times means its Hepatic Cause.

AST $\Rightarrow$ RBC, non specific, all ms $\Rightarrow$ 45 IU

ALT $\Rightarrow$ Slightly more specific $\Rightarrow$ 45 IU

$\Rightarrow$ 6 times $\uparrow$ elevation to ~~can~~ go with liver damage.

GGT "Gamma Glutamyl transaminase" if $\uparrow$ with ALP
it's $\Rightarrow$ Biliary system damage.

also 5 nucleotidase $\uparrow$

GGT only $\uparrow$ $\rightarrow$ Alcoholic

to be sure

if AST : ALT

2 : 1 AST doubling ALT
 $\Rightarrow$ Alcoholic pt.

Hemolytic
Pre Hepatic

Jundice
hepatocellular
Hepatic

Cholestatic
Post Hep

Biliary Pancreatic

LFT

CBC

AST $\times 6$ times
ALT

ALP $\times 2.5$ Normal

AST $\uparrow$
ALT $\uparrow$

ALP $\uparrow < 2.5$

D.D

* Biliary system dis
next steps

U/S if dilatation + stone

Next step MRCP

Next step ERCP

Could be even therapeutic

D.D

- 1- Viral Hepatitis
- 2- Alcoholic
- 3- NASH
- 4- Autoimmune
- 5- Wilson
- 6- $\alpha 1$ Antitrypsin
- 7- Hemochromatosis
- 8- Drugs & Halothane, & methyl dopa
- 9- idiopathic.

- 1- Gall bladder Stone
- 2- Acute Biliary Cholangitis
- 3- Primary sclerosing cholangitis
- 4- pancreatic disorder
- 5- Cholangio Carcinoma

Next Step 8

GGT, ALP: AST ratio

NASH $\Rightarrow$ U/S

iron study.

- epigastric pain radiated to the back Pancreatitis,
Calculi Cholelithiasis.

Fatigue is one of the most exciting Sym. of pt. with liver dis. BC of $\downarrow$ Glycogen $\Rightarrow$ most common complain. One of liver functions is Δ protein synth:

- Albumin 4-8 gm/day Albumin : Globulin
2 : 1

- Clotting factors

- protein S & C

Albumin has No Roll in inv. of Acute liver dis

BC its half life but it does $\downarrow$ with chronicity

- Globulin may $\uparrow$ in Acute Ratio 1:1

~~But~~ with chronicity $\Rightarrow$ reversed ratio

A:G 1:2

- ~~the~~ clotting factors $\Rightarrow$ half life is hours

most sensitive $\rightarrow$ PT 12-13 $\rightarrow$ 20-30 Sec & prolonged in Acute failure

- in Acute failure:

- Ceroplasmin $\uparrow\uparrow$

- Transferrin $\uparrow\uparrow$

* saturation Not level

if Bilirubin level was 6

~~LDH~~ ~~ESR~~ ~~aspartate~~

CBC Hb=6, Rtx: 11%

"Autoimmune hemolytic anemia"

Autoimmune or Rifampicin



Do a
Coombs
test

+

-

- every ↑ in bilirubin level Do a LFT ⇒ AST & ALT
& endocrine function BC liver is responsible
of metabolism of hormones so any disturbance will
lead to ↑ or ↓ in hormones ⇒ Hormonal function disturbed

- any D.M Pt. gets a liver dis leads to unopposed attacks
of Hypo & Hyperglycemia

- any Pt. with liver dis has clots ~~has~~ bc ↓ in protein S &
anti coagulants " & also bleeding tendency " ↓ in clotting
factors "

Hyp E can lead to chronicity in Pt. with chronic liver dis
or ↓ immunity

Hepatology 2

1 1 8

- Symptoms of liver dis

- 1- N/V/A
- 2 itching
- 3- jaundice
- 4- diarrhea "No bile"
- 5- Constipation "electrolyt disturbance"
- 6- Bleeding tendency
- 7- Abd. pain
- 8- disturbance of Consciousness
- 9- loss of Consciousness. BCs

- 1 Hepatic encephalopathy
- 2 Hypoglycemia
- 3 fall down bc of drunken state
- 4- Hg.
- 5- Alcoholic intoxication.

Note $\uparrow$ Ca^{++} & $\downarrow$ K^{++} $\Rightarrow$ Constipation

- investigation of liver dis

CBC, US, MRCP, Biopsy, U/E, Ca^{++} if needed

ESR, CRP, Serum albumin, LFT, ERCP.

When a pt. is symptomatic with $\downarrow$ clotting factors

& Bruis & its necessary to take a biopsy $\rightarrow$

Do a transjugular it has low risk of bleeding.

- 1- disturbance of sleep
 - 2- Hepatic flapping
 - 3- Confusion
 - 4- Ataxia & Hyperreflexia
 - 5- Coma
- all are signs of Hepatic encephalopathy.

The best inv. to reveal Ascitis is U/S, to detect

ascitis by abd. exam. it should be $\uparrow$ 700 ml

U/S should be done every 6 months in Cirrhosis pt. to detect any mass

even Hip. A, E can lead to chronicity, specially in pregnant ladies, immune compromised pts & pre existing liver dis.

- Mechanism of Ascites

1. $\uparrow\uparrow$ in Hydrostatic pressure transudate

2. $\downarrow$ albumin

main Cause.

3. RAS system $\uparrow$ Na & H₂O intravascular $\Rightarrow$ $\uparrow$ Ascites

- Aldosterone antagonist is the main Rx & D.O.C in Ascites of Liver Cirrhosis pts.

- Start with Spironolactone if moderate to severe ascites

- Pt. is Not responding to spironolactone when reaching max. dose 400mg for 72hr. $\Rightarrow$ Refractory ascites.

- Add furosemide "2nd line" after 3 days, but inv. serum K⁺ first BC $\downarrow$ K⁺ + furosemide $\Rightarrow$ Arry. $\Rightarrow$ Stop medication

- Ascites should improve by $\downarrow$ in wt. by 1-1.5kg daily, if 2 max. dos medication & No improvement for 1st week, $\Rightarrow$ T_{ape}

- Spironolactone $\uparrow$ K⁺ but RAS system $\downarrow$ K⁺ $\Rightarrow$ Hypokalemia

- if pt. has a Arry. $\Rightarrow$ Stop medication & T_{ape}.

Ascitis is good media for any ~~inst.~~ inf.
Spontaneous inf. with E. coli the pt. comes with
Sever abd. pain + rigidity
refractory Ascitis Not responding to treatment
Normal WBC
No fever BC of the neutropenia.

The Dx tool is fluid aspiration & inv. the fluid
if WBC $\uparrow\uparrow$ 250,000 $\Rightarrow$ Dx spontaneous bacterial
peritonitis

Complication of Cirrhosis

1 - Congestion in intestine $\rightarrow$ malabsorption & wt. loss
if the Doctor caught the esophageal varis in
an early stage give Carvedol $\rightarrow$ $\downarrow$ intestinal blood supply
Not all splenomegaly leads to Hypersplenism
but every Hypersplenism has a splenomegaly.

2 - Hepatic encephalopathy

it ~~they~~ occurs more in pt with esophageal varis
BC it has a systemic shunt $\Rightarrow$ Blood from intestine directly to
the brain

Es. varises Rx

Prophylaxis if before bleeding $\Rightarrow$ Carvedol 1st prevention
Ligation if after bleeding + Carvedol 2nd prevention

after esp. varises bleeding, insert a nasogastric tube & aspirate all the fluid & blood from the stomach to stop converting the blood to ammonia & worsen the brain state & the pt. may fall into a coma.

- The least severe liver dis. lead to Cirr. & Cancer in Wilson

- Ascitis in liver dis. pt. is a late stage sym. & its a bad prognostic sign.

- Albumin, bilirubin & INR all indicates severity of liver dis.

Hepatology 3

1 / 12

2 of Portal Hypertension

1. Treat the underlying cause
2. B-blocker: propranolol or Carvedilol 12.5 mg ^{selective}
3. if after bleeding $\Rightarrow$ ligation
4. TIPPS

* if a Pt. presented with hemoptysis & BC of esoph. Varices & has cirr. & on B-blocker medication the Pt. will be hypotensive but with low H.R. B.C. of the B-Blocker.

Paroxysmal Nocturnal Urine

HyperCoagulable state with pancytopenia
& Pt. may also have Rt. hypochondrial Pain
& ~~rapidly~~ rapid ascitis.

Budd-Chiari Syndrome

Pt. has Rt. hypochondrial Pain, & rapidly proceeded ascitis.

Esophageal Varices

it can lead to upper GI bleeding which can be presented with Hematemesis mainly, fresh blood per rectum, melena, shocked, died, or anemia without any symptoms.

- bleeding in stomach from a big large varicis ~~pass~~ the blood passes from the stomach to the intestine, normal flora & enzymes ~~can't~~ can't transfer the blood & digest it so it passed as fresh blood.

-in case of the Meckel's diverticulum in terminal ileum ~~with which~~ which has a tissue of gastric mucosa & secretes HCl & digests any blood $\Rightarrow$ So any bleeding in the intestine may be digested & manifested with melena & it's a lower GI bleeding Not upper.

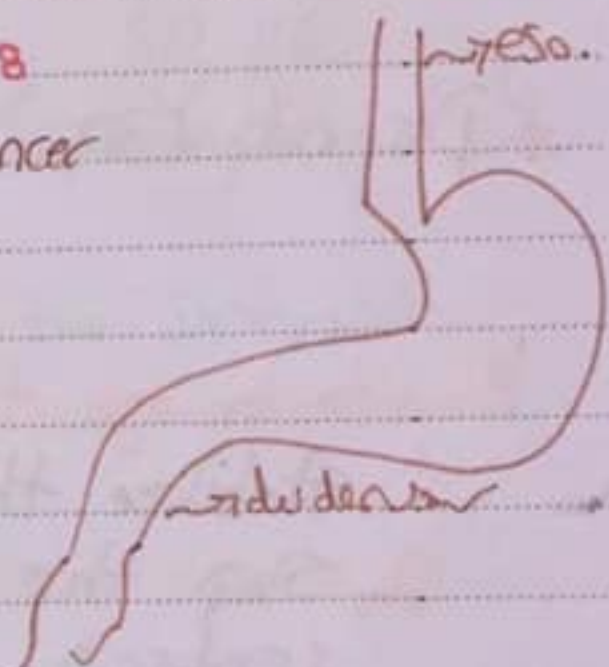
Causes of GI bleeding "upper" &

any "itis" inflammation or infection, Cancer or ulcer in this organs &

gastritis, esophagitis, duodenitis

Eso. gastric Cancer "duodenal" Cancer is very rare //, Aorto-enteric fistula "rare

"severe condition" // any ulcer varices. bleeding disorder or Anti Coagulant medication over dose.



1. peptic ulcer 50%

2. Gastroduodenal erosions 8-15% "gastritis, fistula"

3. esophagitis 5-15%

4. Mallory weiss tear 15% Sudden vomiting without relaxation of cardiac sphincter in Hyperemesis gravidarum, Alcoholic

Self limited, ask about Last normal period "pregnancy" alcohol intake & has there pt. vomits normal gastric Content before ~~the~~ or the blood or was it only blood if yes it's

5. Eso. varices 5-10% Mallory weiss tear!!

- * 1st Step to check the pt. BP
- * Upper GI endoscopy has a window period of 24hr. & it's not the 1st step in management.
- * The most common cause of death of upper GI bleeding cases is MI*
- * Pts. with Cirr. + Portal HPN $\rightarrow$ 80% es. varices
 $\rightarrow$ 20% other causes

How to manage the bleeding &

- 1- stabilize the pt.
 - 2- Stop the bleeding by:
 - 1- endoscopy
 - 2- Drugs
 - 3- Sengstaken tube
 - 2- TIPS
 - 3- prevent the complication "rebleeding"
 - 4- Treat the Cause
- 1- Stabilize the pt.

- 1- maintain the pt. airway clear to prevent pulm. blood aspiration
- 2- Give O₂ if the airway is patent "start with low O₂ concentration"
- 3- restore circulation &
 - insert 2 large bore canula, draw blood for inv. CBC, cross matching. Blood sugar, LFT, U&E, clotting screen
 - ~~by central line~~

✓ prepare 4 units of blood,
give fluid, blood, or plasma. The most fluid recommended is

1 - Free Salt albumin

2 - Normal saline Hypotonic 0.35%

3 - 5% Dextrose Saline especially in the pt. hypoglycemic.

* Try to aspirate the blood from the stomach to prevent ammonia formation

- Continue vital signs monitoring BP, HR

⇒ IV Antibiotic 3rd generation Cephalosporin & proton pump inh.

* There are shavers to improve the prognosis.

* Antibiotic to ↓ the incidence of spontaneous bacterial peritonitis.

* Proton Pump inh. do not give it unless there's an active GI bleeding.
it ↓ the incidence of rebleeding.

- pt. with liver cirrhosis has a high level of Gastrin.
that ↑ the production of HCL. BC it's metabolised in the liver ⇒ ↑ HCL ⇒ ↑ acidity ⇒ Gastric ulcer.

* How to insert Sengstaken Blakemore tube

insert from the nose, to leave the mouth free for, on emergency endotracheal intubation.

it has 2 balloons eso. & Gastric

4 opening 2 for to inflate the gastric & eso. balloon.
& 2 for Suction Eso. & Gastric.

- inflate the Gastric balloon first by 250ml air.
Don't use any sedation in these pt. already deteriorated
from the hepatic encephalopathy.

if any sedation given the pt. may fall into Coma.
make sure the tube is not falsely inserted in the lung
by stethoscope on epigastric area & inflate the gastric
balloon you must hear bubbling, if not try the Rt. axilla
if any bubbling heard $\Rightarrow$ false insertion in the Rt. lung.

2. by the O₂ saturation if radically dropped $\Rightarrow$
false insertion in the lung.

3. Confirm it by X-ray.

- the balloon compress the gastric varices, Complete
the suction, if the bleeding has not stop after
30 min. $\Rightarrow$ inflate the eso. balloon.

- Eso. balloon inflated by 40mmHg. max

- empty the air for 10min. every 3hr. to prevent
eso. necrosis if complete compression continued for 6hr.

* Fresh frozen plasma has all the clotting factor, short half life in the
Cryoprecipitate $\sim$ only 3 $\sim$ long half life in bank

Vit. K. has No roll in Acute Hg, but we give it anyway to prevent
rebleeding & improve Clotting factor formation from the Non cirr. Part
of the liver.

When the Clotting factors that are given is metabolized.

- Who is the candidate pt. of blood transfusion?

- if there is an active bleeding at presentation.

→ give blood when Hb $< 10g$

- if the pt. is stable & has no bleeding &

give blood when Hb $< 7g$

or $< 9g$ in pts. with heart failure.

Hepatology 4

1 / 18

* The most common cause of admission in pt. with Liver Cirrhosis

1 Ascitis "most common"

2 Hepatic encephalopathy.

3 Bleeding disorder "even unexplained anemia"

What are the causes of ascitis in Cirr. pt.?

1 Portal Hypertension

Extravasation of fluid by hydrostatic pressure

2 In late stage Albumin will decrease $\Rightarrow$ No osmosis $\Rightarrow$ fluid extravasation

3 during Cirr. the lymphatics draining inside the liver & outside "extra hepatic" will be obstructed $\Rightarrow$ slight $\uparrow$ in ascitis

4 Prolongation of aldosterone action BC of decrease its metabolism by the liver $\Rightarrow \uparrow$ Ascitis

($\uparrow \uparrow$ Aldosterone secretion $\Rightarrow$ due to decrease in Renal blood flow & RAS system activation. $\Rightarrow \uparrow \uparrow$ Ascitis)

This mechanism is the main cause of ascitis

* ~~any~~ In Liver dis. any hormon may show hyperactivity signs & symptoms without actually increase in its level BC of decrease the metabolism rate by the liver.

* Spironolactone takes time to act BC the presence of ascitis is prolonged & complicated.

any infection $\Rightarrow \uparrow$ cytokines $\Rightarrow \uparrow$ permeability in B.V. $\Rightarrow$ exudative edema with high protein.
inflammation $\nearrow$
malignancy $\nearrow$

⇒ Appearance of ascitic fluid :

- in Cirrosis : Clear, straw colored or light green
- in Malignant dis : Bloody
- in infections : Cloudy
- in Biliary communication : heavy bile staining
- in Lymphatic obstruction : milky white

* Ascitis ^{cases} Can be ~~re~~classified ~~the~~ according to protein level in the ascitic fluid

- exudative "ascitic protein concentration $\geq$ more than 25g/L
- Transudative "ascitic protein concentration less than 25g/L

But it's Not used anymore

- Or can be classified according to serum ascites albumin gradient "SAAG"

low gradient < 1.1

No portal Hypertension

- Bacterial peritonitis
- Neoplasm
- pancreatitis
- Nephrotic syndrom

High gradient > 1.1

portal hypertension

- Cirrhosis without hypoalbuminemia
- CHF
- Budd chiaci syndrom

⇒ How to diff. Blw ascitis causes "H.F.,
Nephrotic syndrom, Liver cirr."

	H.F	Nephrotic	Liver Cirr.
	"unComplicated"	Syndrom	

Serum Albumin	Normal	↓↓	↓↓
Urin Albumin	Normal	↑↑↑	Normal

⇒ Ascitis pt. with liver hepatitis can cause Rt. side Plural effusion

⇒ Lt. side Plural effusion may be ~~caused~~ associated with pancreatitis.

* Unilateral ascitis D.D 8

- 1- TB ascitis
- 2- Ovarian Cyst
- 3- Hydated Cyst

* Shifting dullness should be done in both sides.

- Bowel sounds may be absent ~~with ascitis~~ in ~~ascitis~~ pt. with ascitis, while its always absent in pt. with ~~peritonitis~~ peritonitis.

-Venus hum can be detected even in sever ascitis

-When paracentesis is performed ~~rept~~ replace the fluid that has been aspired with Albumin if the ascitis caused by portal hypertension "Bc the blood vessel permability is intact" While if there were No portal hypertension the albumin will worsen the ascitis "B.V permability is ↑"

*Peritonitis:

2 types : 1 Homogenous bacteria "E.coli", spontaneous with No previous procedures.

2. Heterogenous Bacteria, 2nd to procedure.

Symptoms:

Fever abd. Pain *woody abdomen* tenderness, abdominal signs are mild or absent in 1/3 of pt. +/- hepatic encephalopathy.

IV ~~Cef~~ Cefotaxime +/- Rifampicin

For prevention of recurrent ciprofloxacin or Norflaxacin for life

Prognosis: The mortality rate during 1st year is 50%.

Note* most common electrolyte disturbance among pts. in hospitals is metabolic Alkalosis BC of the diuretics.

Hepatic Encephalopathy

* D.Ds of unconscious Pt. with liver Cirr. &

1. Subdural hematoma

if the pt. was drunk & fall down on his head a hematoma could be formed BC of the decrease of clotting factors "liver cirr." & ↓ in the platelets count "BC of hypersplenism".

2. Delirium tremens

it's an acute confusional state 2nd to sudden stop of alcohol, also occurs after surgery.

3. Alcohol intoxication

4. Wernickes encephalopathy

5. Hypoglycemia

6. Wilson dis.

7. Hepatic encephalopathy.

* Hepatic encephalopathy is 3 types

Type A: Acute hepatic encephalopathy

Type B: or complication after TIPS

Type C on top of liver Cirro.

- Clinical presentation

it has 4 Stages, Brain edema & $\uparrow$ ICP could occur in the end stage "Stage 4"

Signs of hepatic encephalopathy:

- 1- Flapping tremor "Flixion" in the metacarpopharyngeal joints
- 2- Fetor hepaticus

- Signs of liver cell failure in general:

- 1 Confusion
- 2 Ascitis
- 3 Jaundice

* The Dx is done after exclusion the other D.Ds & Normal CT unless the pt. was in stage 4, the a CT may show a brain edema.

* Precipitant factors:

Any Cause lead to $\uparrow$ Ammonia level in the Blood,

- 1- Any GI bleeding even if small amount
- 2- High protein meal

But don't stop protein intake as apart of management in either liver cirr. or Nephrotic syndrom just limit the amount of protein intake.

- 3- Constipation or drug induced Constipation.

Any $\uparrow$ in the transiente time $\uparrow$ Time needed for the food

to pass through mouth to anus), will $\uparrow$ ammonia production from the normal flora.

4 CNS depressant drugs (Benzodiazepines, Barbiturates) in Hepatic encephalopathy there is a up regulation of the Benzodiazepines receptors, so even a low dose will ~~decrease the case~~ ~~worsen~~ $\rightarrow$ worsen the case

5- Paracentesis & TIPPS

6- Infection, especially UTI

7- Acid Base imbalance

Acidosis $\Rightarrow \uparrow$ in H^+ anion $\rightarrow$ Urea & ammonium $\rightarrow$ Ammonia

Alkalosis $\Rightarrow$ Ammonia $\rightarrow$ Urea into release the H^+ anion

So Both Acidosis & Alkalosis $\uparrow$ Ammonia level.

8- Dehydration

BC it Cause an Acid-base imbalance.

9- Hypokalemia

* Constipation, infection, procedures & GIT bleeding are the most common precipitant factors.

Treatment:

1- Remove any precipitant factors, Don't decrease the protein intake

2- Good hydration & correct electrolytes.

3- Lactulose 15-30 ml 3 times/day

in constipated pt. Lactulose given unlimited ~~the~~ till the motion occurs, then fixed 3 times/day.

in refractory cases add Rifaximin 400mg 3 times daily
" it's a non-absorbable oral antibiotic that ↓ numbers of
nitrogen forming gut bacteria.

4. Liver transplantation is indicated if resistant.

emergency cases in Hepato:

1. Hepatic encephalopathy
2. Ascending Cholangitis
3. paracetamol toxicity

In iron deficiency anemia there's a $\downarrow$ in iron saturation & $\uparrow$ in iron capacity.

* Pathophysiology:

it's an Autosomal Recessive disorder in which there is a mutation in HFE gene Chromosome 6 which cause $\downarrow\downarrow$ in hepcidin protein production from the liver, which leads to $\uparrow$ in intestinal absorption of iron, $\uparrow$ in iron capacity & $\uparrow$ in Transferrin saturation ~~which is~~ ~~more~~ ~~than~~ ~~45%~~ more than 45%, with free iron that circulate the body with the blood & precipitate in organs.

The iron precipitate in pt. organs "heart, skin, pancreas, liver, joints & glands", all damage that it caused is irreversable except in heart & skin can be reversable with treatment.

- Hemochromatosis $\uparrow$ risk of hepatocellular carcinoma.
- The cancer risk is Not eliminated even with treatment & venesection or even after liver transplantation.

- Venesection is treatment of choice if the pt. wasn't anemic.
- Desferrioxamine is ~ ~ ~ if the pt. is Anemic.
- "Desferrioxamine"

- Iron precipitate in pituitary gland causes hypopituitarism which causes ~~subfertility~~ sub-fertility & infertility.
- iron precipitate in testis causes testicular enlargement & atrophy in late stage, but doesn't cause infertility.
- ~~iron precipitate in skin~~
- Melanocyte stimulating hormone is part of ACTH →
↑ Melanin → Dark skin.

Hemochromatosis case mainly presented as 8
Male, D.M., Dark skin.

2 Arthritis, Dark skin & subfertility

Hyperpigmentation + vomiting + epigastric pain → Addison

Hemochromatosis cause arthritis mainly in 2nd & 3rd
Metacarpophalangeal joints
+ ChondroCalcinosis which is Ca^{++} deposition in
2nd & 3rd metacarpophalangeal joints cartilage.
→ it's called Pseudo gout

- Hemochromatosis causes impotence BC of testicular involvement, while it ~~can~~ cause infertility or subfertility BC of pituitary gland involvement.

- Liver damage starts when iron level in blood more than 1000 μg . The pt. may be presented with D.M., Arthritis

or subfertility before liver manifestations.

* Hemochromatosis decrease life expectancy by 8-10 years only if the pt. develops DM or liver cirrhosis

* Screening for hemochromatosis is done by Transferrin Saturation in low risk groups, while it's done by Genetic study for HFE gene for high risk groups "1st degree relatives".

* Screening for malignancy in pt. of hemochromatosis is done By:

- 1 - U/S if pt. has liver cirrhosis
- 2 - α Feto protein is No cirrhosis

* Hepatocellular carcinoma is the most common cause of death in hemochromatosis pts.

Treatment:

* Nonpharmacological:

Decrease iron intake

↓ Orange juice intake vit C & Red wine $\uparrow$ Fe^{2+} absorption
Tea $\downarrow$ iron absorption.

* Pharmacological Venesection 500g weekly for 18 months.

monitored by CBC; hematocrit less than 50%, ~~Transferrin~~ ^{Ferritin} ratio less than 40%, Ferritin ratio < 100 $\mu g/dl$

Wilson's disease

- it is an Autosomal recessive disorder characterized by excessive Copper deposition in tissues.

Pathophysiology:

* Defect in ATP7B gene located on chromosome 13 which codes for ~~ceruloplasmin~~ Ceruloplasmin leading to $\uparrow$ in Cu^{++} absorption & $\downarrow$ in its excretion.

* This gene mutation has more than 300 subtypes. Some are mild, some are moderate & some are severe type of Wilson's dis.

* This mutation leads to:

- 1 $\uparrow$ in Cu^{++} absorption
- 2 $\downarrow$ in Cu^{++} excretion
- 3 in 95% of pts. Ceruloplasmin level is low $\rightarrow$ which leads to a high level of free Cu^{++} in serum $\rightarrow$ Cu^{++} deposition in tissues.

- The severe cases of Wilson's dis. has all 3 defects, & mild & moderate cases has 2 out of 3.

- S/o of Wilson's pt. has normal caeruloplasmin level
So normal caeruloplasmin level doesn't exclude
Dx. of Wilson's dis.

- investigations

- Copper level in blood is Not accurate & it's Not ~~not~~ used in Dx of Wilson

* Criteria of Wilson Dx 2 out of 3:

1- Cu⁺⁺ level in 24 hr. Urin collection more than 35 mcg/24hr

2- ↓ Serum caeruloplasmin

3- Kayser-Fleischer ring by slit lamp exam.

- Liver biopsy

- Brain MRI or CT

- ↑ Cu⁺⁺ level in urine >25 mcg/dl after 3 days of penicillamine treatment

- Wilson's pt. may has a ↓ visual acuity BC of Copper deposition in the lens that causes Sunflower Cataract

- Kayser-Fleischer ring doesn't ~~interfer~~ ~~with~~ visual acuity

- When there's a Cu⁺⁺ deposition in lens or Cornea ⇒ there's always a deposition in the Brain even if there's No Neurological symptoms manifested by the pt.

Kayser-Fleischer ring disappear with treatment.

- What are the cases that it could be referred from ophthalmologist to the internal medicine departments
- 1 D.M 2 Hypertension 3 Graves disorder
- 4 Wilson's dis 5 M.S. 6 Behcet's dis.
- 7 Rheumatological disorders.

- Copper deposits in nails cause sky blue discoloration in the distal part of finger.
- Wilson may cause osteoporosis.
- Wilson is the least liver disease that may lead to hepatocellular carcinoma.
- Wilson should be suspected in a pt. with Parkinson below 50 years
- Pt. with jaundice + Neurological manifestations.

Treatment:

- D.O.C
D-penicillamine for life, even during pregnancy
stop only if it caused protein losing nephropathy
" protein in urine $> 3.5 \text{ g/d}$
- Trientine 2.5g/day may be used as an alternative
- Zinc 50mg 3 times daily used more in children
- Liver transplantation in end stage
- Screening for siblings.

Kidney is affected in Wilson by:

- 1- Copper deposition in Renal tubules causes Renal tubular acidosis
- 2- Wilson treatment α -D-penicillamine can cause protein losing nephropathy.

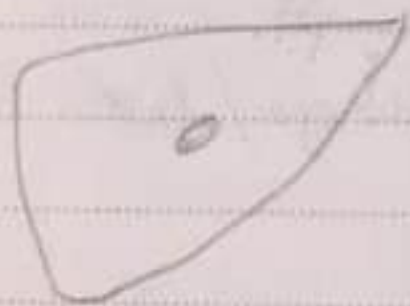
• Deficiency of α 1 antitrypsin •

- Lung alveoli has elastic fibers in its walls to help in lung expansion & collapse during inspiration & expiration.
- These elastic fibers $\downarrow$ normally by ~~age~~ age.
- Elastase enzyme $\downarrow$ elastic fibers $\Rightarrow$
- Liver secretes α 1 antitrypsin which inh. elastase activity.
- Smoking causes $\downarrow$ α 1 antitrypsin activity & $\uparrow$ elastase activity.
- COPD symptoms mainly manifested in pt. who has been smoking for 20 years, package/day $\times$ 20 packg/year, & pt. is >40 yrs.

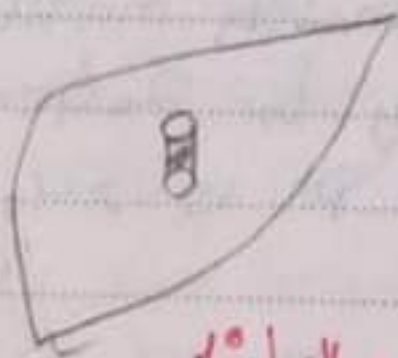
- $\Rightarrow$ COPD symptoms in pt. <40 yr. $\Rightarrow$ α 1-Antitrypsin deficiency or Cadmium exposure daily.
- $\Rightarrow$ Pt. with hyperinflated chest + jaundice & $\uparrow$ elevated liver enzymes $\Rightarrow$ α 1-Antitrypsin deficiency

Autoimmune liver diseases

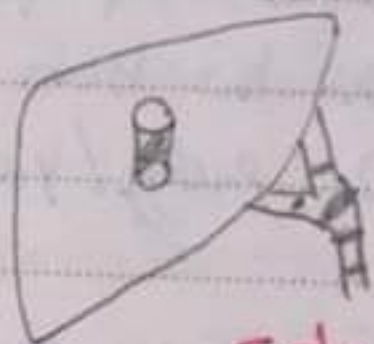
- All has some common features:
 - more common in females
 - more in young & middle aged pt.
 - has a true serology for Ab.
 - has a relapse - remission course.
 - Steroids has roll in treatment "There's exceptions"
 - associated with other Autoimmune dis.
 - have environmental factors, genetic roll, & may be
 - linked to some infections.
 - if a pt. has one Autoimmune dis., you have to ask about other Autoimmune disorders symptoms in history.
- Schmidt syndrome: it's a poly endocrinal failure type 2, pt. has Addison's dis. Graves dis. or hypothyroidism, Myasthenia gravis, pernicious anemia, Coeliac dis., vitiligo, SLE



Autoimmune
Hepatitis



1° biliary
Cirrhosis



Sclerosing
cholangitis

ser Female

Female

male

R: Steroid

Steroid

Steroid

Not effective

C/p: 1. Acute hepatitis

Bile obstruction.

11 Failure: ascites, jaundice
hepatic encephalopathy

* Retention:

- itching

may start years before jaundice

2. Cirrhosis

3. Rare Hepatocellular

Carcinoma

- Jaundice

↑ Cholesterol

Sclerosing Cholangitis 2 types:

1° No history of surgery or malignancy in Biliary system or pancreas
2° if the history

* Steatorrhea ⇒ AkED vit.

it's a large bulky stool difficult to flush away, Contain large amount of fat more than 20g. daily

⇒ Any case of jaundice + itching ⇒ I Biliary Cholangitis till prove otherwise

⇒ in any pt. with jaundice always ask about it there was itching before jaundice

⇒ Cholesterol level ↑↑ with severity of the disease.

Symptoms of vitamin deficiency,

Vit. A: vision disturbance, skin

Vit. K: Bleeding disorder

Vit. E: Skin manifestation,

subfertility, infertility

Vit. D: Bone Pain, Back Pain

osteomalacia, pathological fracture.

LFT: AST ↑↑↑
ALT ↑↑↑
ALP ↑

AST ↑
ALT ↑
ALP ↑↑↑

AST ↑
ALT ↑
ALP ↑↑↑↑

Sero-
logical
test

ANA IgG ↑
ASMA
ALK A
Ad P A

AMA
IgM ↑

p-ANKA

- All the Antibodies are Not specific 100%.
- jaundice + itching + the AMA $\Rightarrow$ Biliary cirrhosis.
- jaundice + itching + pain at Rt. hypochondrial area + malabsorption + the p-ANKA $\Rightarrow$ sclerosing cholangitis.
- Pt. with ↑ AST & ALT, ALP ↑↑↑ + jaundice, imaging showing a stenotic intra & hepatic biliary system $\Rightarrow$ sclerosing cholangitis.

$\Rightarrow$ Autoimmune hepatitis has 3 types:

- 1 Type 1: Classical type, accounts for 80% of the Autoimmune hepatitis cases.
 - associated with HLA-DR4 & HLA-DR3
 - well respond to treatment.
 - ↑ ANA, ↑ ASMA, ↑ IgG.

Type 2: +ve ALCA, No AMA or ASMA

- Poor ~~prognosis~~ prognosis, it's the child type
- Not responded to steroid
- Rx: Liver transplantation with immunosuppressant

Type 3:

- +ve ALPA
- -ve ANA & ASMA

- ~~ve~~ -ve ~~ANA~~ ANA & ASMA doesn't exclude Dx of Autoimmune hepatitis esp. if $\uparrow$ IgG.

- All these type has the same histopathology ~~features~~ features.

- Pt. with Fever, Rt. hypochondrial pain, jaundice No ascitis or hepatic encephalopathy

→ IS it: Acute viral hepatitis, paracetamol toxicity, alcoholic hepatitis, Acute Autoimmune hepatitis?!

- ask the pt. about alcohol & Drug history.

- viral screen, which may show a +ve hepc or E as a false +ve in Autoimmune hepatitis.

→ Associations:

- 1- Urticarial Rash & vitiligo
- 2- Ulcerative Colitis
- 3- Arthralgia & migrating polyarthritis
- 4- kerato-conjunctivitis sicca

5- pernicious anemia

7- Autoimmune thyroiditis

9- Glomerulonephritis

6- ILD

8- DM1

- Rheumatoid factor is not specific to any dis. it may be true in so many diseases. ~~so~~ so don't ask for RF alone in investigation Bc it Dx Nothing & exclude ~~nothing~~ Nothing.

⇒ Azathioprine ~~is~~ has No teratogenic effect & Can be given during pregnancy.

⇒ Azathioprine S/E:

1 Bone marrow depression

2- lymphoma

3 Melanoma

4 Pancytopenia "Plt. is occurring first"

Type of Granulomatous Liver disease

Chronic inflammation with fibrosis & chronic inflammatory cells deposition

1- Sarcoidosis

Non Caseating granuloma, causes hepatosplenomegaly, lymphadenopathy & portal hypertension.

2 Schistosomiasis Non Caseating

3- T.B Caseating

4- Drug induced

5- Primary Biliary Cirrhosis

Type 2 Autoimmune hepatitis ~~not~~ which is resistance to steroids may for granuloma

1° Biliary Cholangitis «Cirrhosis»

- This dis. has been referred to as a 1° Biliary Cholangitis w/out Cirrhosis lately BC it doesn't lead to cirrhosis in all pts.
- Portal hypertension may occur even before cirrhosis by the swollen hepatocyte leading to occlusion, in the space of dis. leading to portal hypertension
- PT is elevated BC of vit. K deficiency
- low albumin levels BC of the malabsorption
- if ~~AMA~~ AMA wasn't detected is a suspected case of 1° Biliary Cholangitis, look for IgM level if it wasn't elevated No 1° Biliary Cholangitis

*Treatment:

- Antihistamine is the best drug to treat the pruritus resulted from 1° Biliary Cholangitis
- Sertraline || selective serotonin reuptake inhibitor «Antidepressant» is used to ~~to~~ to treat pruritus.
- Cholestyramine is the main symptom required treatment its effect start after 2 months & the pt. must be informed that the pruritus is not going to resolve directly

- Ursodeoxycholic acid ↓ rate of apoptosis, ~~solubility~~ & improves LFT. after 6 months on treatment LFT will show ↓

- Bisphosphonates is osteoclast inhibitor, given in osteoporosis & malignant cases of osteoporosis & for to Rx hypercalcaemia.

- This drug could cause severe esophagitis the pt. should take while sitting in 90° & with large amount of water.

⇒ if a known case of Biliary Cholangitis complained from anaemia ⇒ suspect coliac disease.

- 5% of pts. with UC have PSC & 80% of pts. with PSC have UC

When both UC & PSC is coexisting in a pt. ⇒ ↑ risk of both Cholangiocarcinoma & Colorectal Cancer.

- Intermittent jaundice

Bile accumulate above the site of adhesion of the Biliary system caused jaundice bc of the obstruction, then the wt.

of Bile leads to reopening of Bile ducts $\rightarrow$
 Improve in jaundice symptoms $\rightarrow$ readhesion in Bile
 ducts $\rightarrow$ Bile accumulation $\rightarrow$ jaundice

$\Rightarrow$ intermittent jaundice D.O.:

1. hemolytic anemia
2. Multiple Gall Bladder stones.
3. Sclerosing Cholangitis

$\Rightarrow$ even in Child - Pugh C & end stage liver cirrhosis
 the pt. may haven't jaundice.

in PSC AST - ALT is elevated but less than 6 times

$\Rightarrow$ Chronic pancreatitis : is caused by recurrent fibrosis
 in CBD causing closure in the pancreatic duct $\rightarrow$
 Auto digestion $\rightarrow$ recurrent Acute pancreatitis $\rightarrow$ Chronic
 pancreatitis.

- Acute pancreatitis is Not PreCancerous

- chronic $\sim$ is ~~not~~ preCancerous, But its
~~re~~reversible

- Osteoporosis is Dx by DEXA scan for #pt-3 hips &
~~lumbar spine~~ lumbar spine " DEXA $\Rightarrow$ ~~not~~ Dual energy

- X-Ray ~~absorptiometry~~ absorptiometry "

Ca^{++} , PO_4^{3-} & ALP $\approx$ normal

- pt. with Osteoporosis Rx with Bisphosphonates.

- Cholangiocarcinoma survival rate is 1 year. even with early
 Dx.

Paracetamol poisoning

- Paracetamol is metabolised in liver, by conjugation of the toxic material to convert it to non-toxic material in high dose, CYP450 enzyme converts the paracetamol to N-acetyl-p-benzoquinone imine which is toxic. But the Glutathione which is an antioxidant, will convert it to Cysteine or mercaptopyrine which isn't toxic.
- With large dose of paracetamol or pre-existing liver disease, the body will run out of the stored Glutathione, & the N-acetyl-p-benzoquinone imine will accumulate in the body causing hepatocellular damage, then renal failure.
- Gastric lavage is better in pt. with large dose, Bc the drug will accumulate together & form a large ~~mass~~ ~~bulge~~ ~~which~~ which can't pass through the pylorus.
- Best time to measure the paracetamol in blood is after 4h. of digestion.
- The Rx is either N-acetyl-Cysteine or ^{methionine} ~~Glutathione~~ orally. If there's No N-Acetyl Cysteine or the pt. has allergy from it give ~~Glutathione~~ orally.
methionine

* Risk of increase toxicity of Paracetamol:

- 1- Anorexia nervosa
- 2- Alcoholics or preexist liver dis.
- 3- on liver enzyme inducers rifampicin, phenytoin, Carbamazepine
- 4- HIV pt.

- NAC is Not given to all pt. Bc it could cause Anaphylactic Shock,

measure paracetamol level in blood after 4h. of ingestion, & plotted on Matthew - Rumack nomogram, if paracetamol level was more than 200 mg/ml give NAC.

- after 12 - 16 h. of paracetamol ingestion NAC is less effective

- pt. with paracetamol toxicity whose known to ~~not~~ have hep. C or B or pre-existing liver disease, is Not managed the same as other pts., Bc in those pts. even low level of paracetamol can cause serious damage

- PT is more accurate indicator for severity more than AST & ALT

Level of Bilirubin indicates ~~severity~~ ~~severity~~ severity

Level of lactic acid indicates severity

Renal failure // High Creatinine, indicates severity

- Kings College hospital criteria in acute liver failure:

- Arterial pH < 7.3 24h after ingestion

or All of the following:

- Prothrombin time $> 100s$

- Creatinine $> 300 \mu mol/L$

- Grade 3 or 4 encephalopathy

} in paracetamol induced liver failure.

Non paracetamol liver failure:

- PT $> 100s$

or 3 out of 5 of the following:

1- Drug induced liver failure

2- Age < 16 or > 40 yrs.

3- > 1 wk. from 1st jaundice to encephalopathy

4- PT $> 50s$

5- Bilirubin $\geq 30 \mu mol/L$.

AST & ALT is Not indicators for severity.

- While giving NAC monitor the Bp, temp, & allergic ~~reaction~~ reaction

if the pt. developed an allergy while receiving the NAC
Don't stop the medication, just decrease the rate of infusion

if the Allergic reaction ~~does~~ doesn't ~~stop~~ improve
Stop medication & give ~~Antihistamine~~ Antihistamin.

- then return the medication but with slower rate.
- if the allergic reaction doesn't improve, stop NAC & put the pt. on methionine ~~orally~~, orally.
 - IV fluid in the pt. has hypotension Bp < 90/60 mmHg.

Jaundice

Bilirubin metabolism

RBCs break down after 120 days → Haemoglobin

Globin

Haem

Fe²⁺

• hepatocyte

• uptake,

• Conjugation

• releases,

Conjugation

Bilirubin

• indirect

• unconjugated

• haemo bilir.

• Non water

soluble

Conjugated Bilirubin

2% of bilirubin
 if excreted in
 enterohexetic

90% Sterobilirogen

10% of sterobilirogen is
converted to
Urobilirogen

3% Urobilirogen

Notes:

- Duodenum has low counts of Bacteria if $> 10^3 \Rightarrow$ overgrowth of Bacteria over growth Syndrome

- The intestine Bacteria oxidate bilirubin & turn it to Stercobilirubin
- 90% of Stercobilirubin passes through stool gives the stool brown color.
- ~~10%~~ ↑ in Stercobilirubin → dark brown stool
- 10% of Stercobilirubin convert into urobilinogen in the intestine & absorbed from intestine to liver
- 3% of absorbed urobilinogen is excreted by kidney "it's water soluble"
- presence of urobilinogen in the urine exclude Biliary obstruction
- the other 7% of urobilinogen is released into the intestine again
- Urobilinogen is Not responsible for the color of urine. Urochrome is responsible for urine color.
- Bilirubin is carried in blood with albumin, & it can be secreted by kidney, BC Albumin is -ve charge

Hemolytic jaundice

- ↑ in RBC's destruction → ↑ unconjugated Bilirubin
- Liver can conjugate more than its normal level up to 6 times

- ↑ in Conjugated Bilirubin → ↑ Stercobilinogen → Dark Brown stool
- ↑ in urobilinogen in urine
- ↑ in unconjugated Bilirubin in blood causing jaundice. But No Bilirubin in urine BC all the Bilirubin is unconjugated → so it can pass to the urine
- ↑ RBC's destruction → ↑ heme " Fe^{2+} " in the Blood, → ↓ ~~Haptoglobin~~ in Free haptoglobin will be occupied by Fe^{2+}
- ↑ in Free " Fe^{2+} " → ~~can~~ which ~~damage~~ damage the kidneys. First it cause shedding in tubules epithelium → ~~the~~ Causing Dark urine, Then it cause hemoglobinuria.
- every RBC destruction ~~can~~ releases K^+ & LDH in the serum → ↑ LDH & hyperkalemia.
- There's difference B/w hemolysis & hemolytic anemia. Bone marrow can compensate any hemolysis up to 10 times it's normal.

~~Hemolysis~~

~~Hemolysis can be compensated up to 10 times~~

- When RBC's life span reach 15 days, the hemolysis could be significant & cause a hemolytic anemia

Cholestatic jaundice.

- Caused by obstruction in Bile ducts intra or extra hepatic.
- mainly Direct Bilirubin $\rightarrow$ No stercobilinogen $\rightarrow$ ~~pale~~ pale stool
- Direct Bilirubin which is water soluble $\rightarrow$ $\uparrow$ Bilirubin in urine

jaundice + Anemia + Tachycardia $\Rightarrow$ hemolytic jaundice

$\sim$ + $\sim$ + Bradycardia + itching $\Rightarrow$ Obstructive jaundice

$\sim$ + Parotid enlargement + Tachycardia $\Rightarrow$ hepatocellular.

jaundice + extrapyramidal manifestation $\Rightarrow$ Wilson's dis.

Case 8

- pt. with recurrent attacks of jaundice with family history to the same illness, $\uparrow$ Alkaline phosphatase, Abdominal pain, $\rightarrow$ U/S revealed $\Rightarrow$ Stone.

he has severe anemia, -ve Coombs test,

$\uparrow$ in both Direct & indirect Bilirubin

He has cholestasis caused by the stone

he has $\uparrow$ K^+ & LDH & $\downarrow$ haptoglobin, ~~the~~ all indicates hemolysis

Any hemolytic anemia can induce pigmentary stone

"at any hemolysis the liver $\uparrow$ conjugated activity up to 6 times its normal level $\rightarrow \uparrow$ direct bilirubin $\rightarrow \uparrow$ Bile Viscosity $\rightarrow$ Pigmentary Stone."

- It happened mainly with hereditary spherocytosis. So in its treatment we do Splenectomy first to $\downarrow$ rate of hemolysis, then Cholecystectomy. If Cholecystectomy was performed first the stone will form in the CBD leading to ascending cholangitis.
- in case of hemolytic jaundice imaging may show gall bladder stone $\Rightarrow$ pigmentary stone.

Alcoholic Liver disease.

- Heavy drinkers $\Rightarrow$ 4 days/week for male
3 days/week for female
- Acute Alcoholic hepatitis can occur ~~to~~ after first $\&$ ingestion of alcohol
- Female & obese pts. ~~are~~ are more likely to have alcohol toxicity Bc of redistribution of $\&$ Alcohol by fat
- if INR $> 1.7 \Rightarrow$ Admit the pt.
- Albumin level is normal in both fatty liver & acute alcoholic hepatitis

alcoholic pts. with liver cirrhosis or hepatic failure are candidates for liver transplantation if they stop drinking.

How to diff. B/w alcoholic & alcoholism?

ask the pt. those questions:

- هل فيه يوم شربت كحول أول ما فقت من النوم؟
هل تحس بالذنب؟

- هل مارتيك مشاكل أسرية أو مع الشرطة بسبب الكحول؟
هل عليك شئ يشربك للكحول؟

- if the pt. answers 2 questions ~~by~~ with Yes $\Rightarrow$ Alcoholism
- Alcoholism pt. ~~will~~ will have severe withdrawal symptoms if they stopped alcohol suddenly
- Chlordiazepoxide is given to prevent alcohol withdrawal symptoms

* Alcohol effects on CVS:

1. Alcohol $\uparrow$ sensitivity ~~for~~ of Catecholamines receptors
Causes $\rightarrow$ ~~thickened~~ Slightly tachycardia, $\uparrow$ vasospasm,
 $\uparrow$ H.R $\Rightarrow$ leading to hypertension
2. $\uparrow$ Dilated Cardiomyopathy, BC it $\uparrow$ sensitivity to Adrenal
which cause remodeling & $\uparrow$ Apoptosis rate
3. Arrhythmogenic effect

*

* Alcohol effect on endocrine s:

- The Alcohol ~~ind~~ induce hypoglycemia
it decrease insulin effect, & ~~can~~ mask hypoglycemia symptoms
- Alcohol may cause D.H, BC it may lead to pancreatitis
- Alcohol can induce all ~~the~~ cancers
- it has teratogenic effect, & may induce abortion.
- It may cause slight improvement in lipid profile.

Treatment of NASH:

1. ~~There~~ Rx of D.H

2. Statins & lipid lowering agents

Hepatology 7

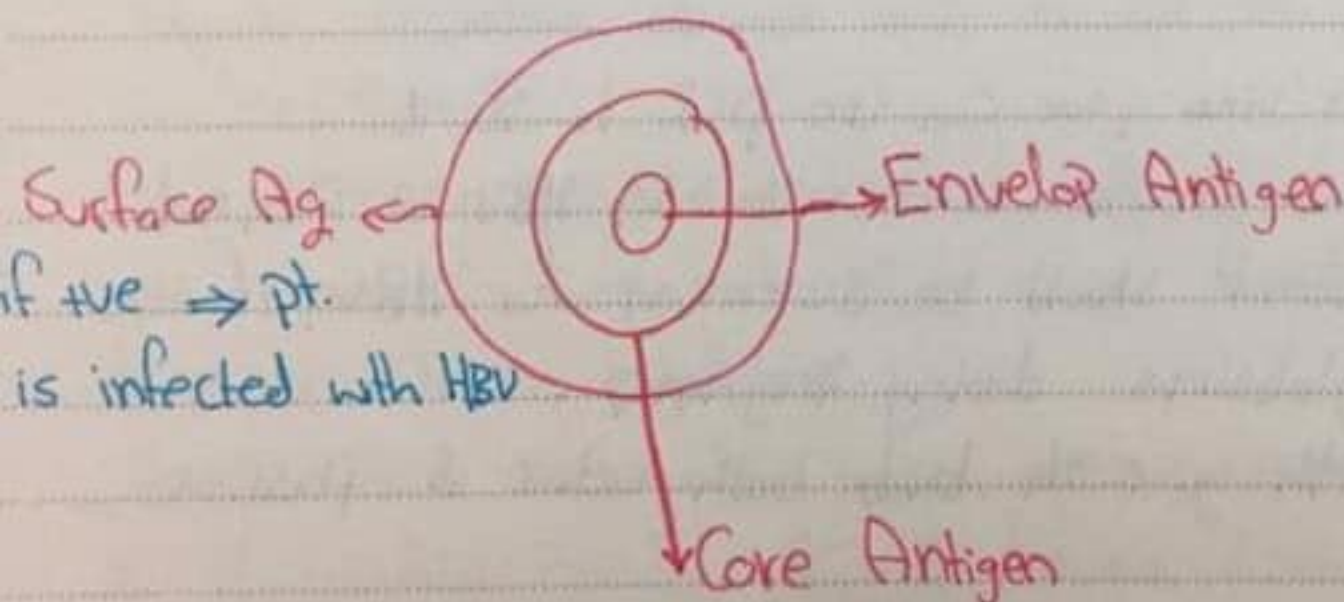
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- hepatitis E virus can cause chronic hepatitis in specific circumstances & pregnancy, kidney transplant & of the immunosuppressant drugs.
- All hepatitis viruses cause mild Acute hepatitis less than 6 months duration.
- Any case coming from ^{Acute} hepatitis like ~~any~~ symptoms do viral screen.
- after Acute hepatitis, all the hepatocytes are ~~swallowed~~ which cause closure in the intra capillary caneculi $\rightarrow$ indirect cholestasis
hepatocyte failed to secrete the conjugated Bilirubin $\rightarrow$ $\uparrow$ Bilirubin in blood appears after 10-15 day
- Acute hepatitis always mild except ~~for~~ with hep B or hep B + D.
- hep B Acute hepatitis is severe $\rightarrow$ ~~the~~ if the pt. got good medical care, it will be cured & ~~that~~ Doesn't ~~become~~ chronic hepatitis
- Hep C Acute ~~in~~ hepatitis? is mild, unnoticed, & if the pt. is Not treated it will become Chronic hepatitis
- AST & ALT doesn't predict severity
- INR ~~increases~~ > 1.7 admit pt.
- Bilirubin if very high indicate severity

- During acute hepatitis treatment, Antiviral is given for Hep. C only.
- Antiviral therapy is given in Acute hepatitis B infection in specific cases e.g. Alcoholic pts., pre-existing liver dis., old age, HIV ~~and~~ & if Co-existing hep B & D infection.
- Hepatitis > 6 months in duration $\Rightarrow$ chronic hepatitis
- Chronic hepatitis may be asymptomatic, ~~but~~ & liver start to Cirrhosis ~~and~~, the normal part of liver can compensate the liver function until 2/3 of liver become cirrhotic $\Rightarrow$ De-compensated liver Cirrhosis $\Rightarrow$ Ascites, jaundice, hepatic encephalopathy
- Hepatitis E virus can lead to chronic hepatitis but it has low risk to hepatocellular carcinoma.
- U/S should be done to pts. with liver cirrhosis every 6 months
- HBV is DNA virus, we can use PCR to Dx. it.
- the most common transmission route in HBV is perinatal
- Any pregnant female should be screening for HBV, if +ve give immunoglobulins during pregnancy.
- after child birth give the baby both active & passive vaccination
- C-section doesn't reduce risk of HBV or HIV transmission ~~to~~ to the baby

- HEV can transmitted by blood & Blood products
- in HBV infection screening is done by serology "Hepatitis B surface antigen" every 6-12 months if the virus is active start treatment
- in HBV screening for hepatocellular carcinoma is done by α -fetoprotein & U/S even before Cirrhosis.
- During screening by U/S if there were any mass, check α -fetoprotein level if it was $\uparrow\uparrow$ take a biopsy
- HCV treatment:
 - interferon + ribavirin $\Rightarrow$ 60% clearance old treatment
 - ledipasvir + sofosbuvir $\Rightarrow$ 100% clearance for 3 months

HBV



Core Ag is Not found in the serum, only seen in Liver biopsy,

Anti: Core HB Immungolbin "IgM" $\Rightarrow$ Acute infection
 Anti: Core HB ~ IgG $\Rightarrow$ Chronic infection

- Surface Ag is +ve for 5-6 months, then it become -ve which called "serological gap" window period, Do Anti HBc serology or HBV PCR. titer
- hepatitis envelop antigen if it was high in serum predicts ↑ in HBV replication & ↑ infectivity
- hepatitis envelop antibody, high levels in serum predicts low level of HBV replication & ↓ infectivity
- in Pt. ~~see~~ with the HBV check ALT if it was high start treatment ~~for~~

Acute HBV	Chronic HBV	immunity	previous inf.	Vaccine
HBs Ag HBc Ab IgM	HBs Ag Hbe Ab IgG	HBs Ab HBc Ab ₂ "IgG"	HBc Ab "IgG"	HBs Ab

- Rx of Chronic HBV: interferon standard 3 times/week or PEGylated 1/week
- Interferon is C/I in Pregnancy, malignancy, lactation, pancytopenia, decompensated cirrhosis.
- Lamivudine ~~is effective~~ has same effect on all HBV genotype
- Lamivudine is taken for life.

- Lamivudine & adefovir cause Renal impairment,
Do Renal function test before ~~start~~ prescribing the medication
& with the follow ups.
- after a needle stick accident from a HBV +ve pt.
Do HBs Ab titer if it was $>100 \Rightarrow$ No need for
Immunoglobulin or Vaccination
if it was $10-100 \Rightarrow$ take immunoglobulin
if below $10 \Rightarrow$ take immunoglobulin & booster dose
of vaccination